



# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 3H270530 2 WO PCT/MN		<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. — PCT/EP 03/13302	International filing date (day/month/year) 26.11.2003	Priority date (day/month/year) 28.11.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/192, A61K31/216, A61K31/195, A61P3/00, A61K31/155		
Applicant FOURNIER LABORATORIES IRELAND LIMITED et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:
- I ☒ Basis of the opinion
  - II ☐ Priority
  - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
  - IV ☒ Lack of unity of invention
  - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
  - VI ☐ Certain documents cited
  - VII ☐ Certain defects in the international application
  - VIII ☐ Certain observations on the international application

Date of submission of the demand  28.06.2004	Date of completion of this report  19.04.2005
Name and mailing address of the international preliminary examining authority:   European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer  Leherte, C  Telephone No. +31 70 340-2748  

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**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-14 as originally filed

**Claims, Numbers**

1-17 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

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**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
- ☐ the entire international application,
  - ☒ claims Nos. 1, 4-17  
because:
    - ☒ the said international application, or the said claims Nos. 11-17 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination (specify):  
**see separate sheet**
    - ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
    - ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
    - ☒ no international search report has been established for the said claims Nos. 1, 4-17 (partially)
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- ☐ the written form has not been furnished or does not comply with the Standard.
  - ☐ the computer readable form has not been furnished or does not comply with the Standard.

**IV. Lack of unity of invention**

1. In response to the invitation to restrict or pay additional fees, the applicant has:
- ☐ restricted the claims.
  - ☐ paid additional fees.
  - ☐ paid additional fees under protest.
  - ☒ neither restricted nor paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
- ☐ complied with.
  - ☐ not complied with for the following reasons:
4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

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- ☐ all parts.
- ☒ the parts relating to claims Nos. 1, 4-10, 11-17 (partially) .

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes: Claims	
	No: Claims	1, 4-17
Inventive step (IS)	Yes: Claims	
	No: Claims	1, 4-17
Industrial applicability (IA)	Yes: Claims	
	No: Claims	see separate sheet

**2. Citations and explanations**

**see separate sheet**

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**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The attention of the applicant is drawn to the fact that for the present application only an incomplete search has been carried out (see sheet PCT/ISA/210, and in particular the last paragraph). The examination will be carried out accordingly.

Claims 11-17 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

**Re Item IV**

**Lack of unity of invention**

The following documents are referred to in this communication.

- D1: WO 99 40904
- D2: DE SILVA S.R. ET AL: 'Metformin and clofibrate in maturity onset diabetes mellitus: Advantages of combined treatment.'
- D3: CHEMICAL ABSTRACTS, vol. 133, no. 15, 9 October 2000; abstract no. 202853
- D4: FR-A-2 275 199

The International Preliminary Examination Authority agrees with the objection for lack of unity raised by the by the International Search Authority, the reasons for the objection being as follows:

The problems to be solved by the present invention are the decrease of serum triglycerides, the treatment of the metabolic syndrome and the treatment of obesity.

The proposed solution is the use of a PPAR-alpha agonist and metformin for the manufacture of a pharmaceutical formulation for those applications.

All these diseases are related to elevated triglycerides levels (see page 3, line 11-line 29).

The treatment of hypertriglyceridemia represents the technical feature which may, a priori,

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unify the different therapeutic uses mentioned above.

The fact that combinations of PPAR-alpha agonists and metformin (or fibrates-metformin salts) lower triglycerides levels is already disclosed. See for example :

- D1: page 9, Table 1
- D2: page 225, table IB
- D3: abstract
- D4: page 6, table II

The idea to use combinations of a PPAR-alpha agonist and metformin for decreasing serum triglycerides is not novel and can therefore not fulfil the role of special technical feature in the sense of Rule 13.2 PCT.

In the present application no further technical feature(s) can be identified which may be regarded as a "special technical feature" involved in the technical relationship between the different inventions.

Consequently, the present application lacks unity of invention and the different solutions not belonging to a common inventive concept are detailed as the different inventions listed hereafter:

- I. Use of a PPAR-alpha agonist and metformin for the manufacture of a pharmaceutical formulation for decreasing serum triglycerides
- II. Use of a PPAR-alpha agonist and metformin for the manufacture of a pharmaceutical formulation for the treatment of metabolic syndrome
- III. Use of a PPAR-alpha agonist and metformin for the manufacture of a pharmaceutical formulation for the treatment of obesity

Each of the inventions listed is a distinct invention, characterised by its own special technical feature, defining the contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

As the applicant has not payed additional examination fees, the report will be formulated for the first invention only.

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability;**

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**citations and explanations supporting such statement**

Attention is drawn to the fact that the present statement expressed as to novelty, inventive step and industrial applicability refers only to matter for which an International Search Report has been drawn up (i.e. only for combinations of metformin with gemfibrozil, fenofibrate, benzaifibrate, clofibrate, ciprofibrate and fenofibric acid).

**1) INDUSTRIAL APPLICABILITY**

Present claims 11-17 involve compositions or substances in a method of treatment of the human/animal body. For the assessment of such claims on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**2) NOVELTY**

The subject-matter of claims 1 and 4-17 is not new in the sense of Article 33 (2) PCT. Documents D1, D2, D3 and D4 already disclose the effect of combinations of PPAR-alpha agonists and metformin (or fibrate-metformin salts) on the level of serum triglycerides.

**3) INVENTIVE STEP**

The present application does not meet the requirements of Article 33 PCT, because the subject-matter of claims 1 and 4-17, if novel at all, appears to be an obvious alternative over documents D1, D2, D3 and D4 and therefore does not involve an inventive step in the sense of Article 33(3) PCT.

And this because, even if some of the PPAR-alpha agonists of the present invention have not been mentioned in combination with metformin in the prior art, it would be obvious to the skilled man to try to replace one PPAR-alpha agonist by another one.